IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of: Jeffrey L. Browning *et al.*

Serial No.: 09/931,402

Filed: August 16, 2001

For: *Anti-Lymphotoxin-Beta Receptor Antibodies as Anti-Tumor Agents*

Attorney Docket No.: BINB185CPUSDV

Group Art Unit: 1642

Examiner: YAEN, CHRISTOPHER H

Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

CERTIFICATION UNDER 37 CFR 1.10

Date of Deposit: May 3, 2004 Mailing Label Number: EL 982738090 US

I hereby certify that this 37 CFR 1.53(d) request and the documents referred to therein as enclosed are being deposited with the United States Postal Service on the date indicated above in an envelope as "Express Mail Post Office to Addressee" service under 37 CFR 1.10 and addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Cristin E. Howley
Name of Person Mailing Paper

Signature of Person Mailing Paper

INFORMATION DISCLOSURE STATEMENT

Dear Sir:

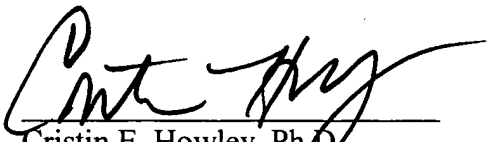
The present application is a Divisional Application of U.S. Serial No. 08/875,560, filed July 25, 1997 (Atty. Docket No. BINB185CPUS). The majority of the references listed on the enclosed PTO Form SB-08 have been previously cited by or submitted to the Office in the prior application and, in accordance with 37 CFR §1.98(d), copies of references A1-B2,

B4-D6 are not enclosed, but will be provided upon request. The remaining reference B3 has not been previously cited and is enclosed herewith.

This statement is not to be interpreted as a representation that the cited publications are material, that an exhaustive search has been conducted, or that no other relevant information exists. Nor shall the citation of any publication herein be construed *per se* as a representation that such publication is prior art. Moreover, Applicants understand that the Examiner will make an independent evaluation of the cited publications.

In accordance with 37 CFR §1.97(c)(2) and §1.17(p), please charge the $180.00 submission fee to our Deposit Order Account No. 12-0080. Please charge any necessary additional fees or credit any overpayments to our Deposit Order Account No. 12-0080.

Respectfully submitted,
LAHIVE & COCKFIELD, LLP



Cristin E. Howley, Ph.D.
Registration No. 55,281
Agent for Applicants

28 State Street
Boston, MA 02109
(617) 227-7400

Date: May 3, 2004

AEM/CEH/cas

PTO/SB/08a/b (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet 1 of 4

Complete if Known	
Application Number	09/931,402
Filing Date	August 16, 2001
First Named Inventor	Jeffrey L. Browning
Art Unit	1642
Examiner Name	YAEN, CHRISTOPHER H
Attorney Docket Number	BINB185CPUSDV

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Document Number: Number-Kind Code[2] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.[1]	Foreign Patent Document: Country Code[3]-Number[4]-Kind Code[5] (*if known*)	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T[6]
	A1	WO 94/13808 A2	06-23-1994	BIOGEN INC		
	A2	WO 92/00329 A1	01-09-1992	BIOGEN INC		

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. [1] Applicant's unique citation designation number (optional). [2] See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. [3] Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). [4] For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. [5] Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. [6] Applicant is to place a check mark here if English language Translation is attached.

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	A3	Alderson, Mark R., 1994, International Immunology, 6:1799-1806, "Regulation of Apoptosis and T cell activation by Fas-specific mAb".	
	A4	Androlewicz, Matthew, J. of Biological Chem., 1992, 267:2542-2547, "Lymphotoxin Is Expressed as a Heteromeric Complex with a Distinct 33-kDa Glycoprotein on the surface of an Activated Human T Cell Hybridoma".	
	A5	Arulanandam, Antonio R., 1993, J. Exp. Med., 177:1439-1450, "A Soluble Multimeric Recombinant CD2 Protein Identifies CD48 as a Low Affinity Ligand for Human CD2: Divergence of CD2 Ligands during the Evolution of Humans and Mice".	
	A6	Bernstein, David, 1993, Antiviral Research, 20:45-55, "Effects of therapy with an immunomodulator (imiquimod,R-837) along and with acyclovir on genital HSV-2 infection in guinea-pigs when begun after lesion development".	
	A7	Browning, Jeffrey, Androlewicz, Matthew et al., 1991, J. of Immunology, 147:1230-1237, "Lymphotoxin and an Associated 33-kDa Glycoprotein Are Expressed on the Surface of an Activated Human T Cell Hybridoma".	
	A8	Browning, Jeffrey and Douglas, Irene et al., 1995, J. of Immunology, 154:33-46, "Use of Specific Monoclonal Antibodies and Soluble Receptors".	
	A9	Browning, Jeffrey and Ngam-ek, Apinya et al., 1993, Cell, 72:847-856, "Lymphotoxin Beta, a Novel Member of the TNGF Family that Forms a Heteromeric Complex with Lymphotoxin on the Cell Surface".	

Examiner Signature		Date Considered	

PTO/SB/08a/b (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet	2	of	4

Complete if Known	
Application Number	09/931,402
Filing Date	August 16, 2001
First Named Inventor	Jeffrey L. Browning
Art Unit	1642
Examiner Name	YAEN, CHRISTOPHER H
Attorney Docket Number	BINB185CPUSDV

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	B1	Browning, Jeffrey and Ribolini, Ann, 1989, J. of Immunol., 143:1859-1867, "Studies on the Differing Effects of Tumor Necrosis Factor and Lymphotoxin on the Growth of Several Human Tumor Lines".	
	B2	Crowne, Paul, VanArsdale, Todd, et al., 1994, J. of Immunol. Methods, 168:79-89, "Production of lymphotoxin (LTalpha) and a Soluble dimeric form of its receptor using the baculovirus expression system".	
	B3	Browning, J. *et al.* The 9th International Congress of Immunology, San Francisco, July 23-29, 1995, "Signalling through the lymphotoxin-beta receptor in conjunction with interferon-gamma induces the death of a human tumor line.	
	B4	Crowne, Paul, VanArsdale, Todd et al., 1994, Science, 264:707-710, "A Lymphotoxin Beta Specific Receptor".	
	B5	Dhein, Jenset al., 1992, J. of Immunol., 149:3166-3173, "Induction of Apoptosis By Monoclonal Antibody Anti-APO-1 Class Switch Variants Is Dependent On Cross-Linking of APO-1 Cell Surface Antigens".	
	B6	Dighe, Anand et al., 1994, Immunity, 1:447-456, "Enhanced In Vivo Growth and Resistance to Rejectionof Tumor Cells Expressing Dominant Negative IFNy Receptors".	
	B7	Duzgunes, Nejat et al., 1992, J. of Cell Biochem., 16E:77, "Liposome Targeting To HIV-Infected Cells Via Recombinant Soluble CD4 and CD4-IgG".	
	B8	Eppstein, Deborah, 1985, Proc natl Acad. Sci., 82:3688-3692, "Biological activity of liposome-encapsulated murine interferon y is mediated by a cell membrane receptor".	
	B9	Fukushima, Keiko et al., 1993, Arch. Biochem. Biophys., 304:144-153, "N- Linked Sugar Chain Structure of Recombinant Human Lymphotoxin Produced by CHO Cells: The Functional Role of Carbohydrate as to Its Lectin-like Character and Clearacne Velocity".	
	B10	Havell, Edward et al., 1988, J. Exp. Med., 167:1067-1085, "The Anittumor Function of Tumor Necrosis Factor(TNF)".	
	B11	Hwang et al., 1980, Pro. Natl. Acad. Sci., 77:4030-4034, "Hepatic uptake and degradation of unilamellar sphingomyelin/cholesterol liposomes: A kinetic study".	
	B12	Johne, Bert et al., 1993, J. Immun.Methods, 160:191-198, "Epitope mapping and binding kinetics of monoclonal antibodies studied by real time biospecific interaction . . . ".	
	B13	Juraskova, Vera et al., 1992, Eur. J. Pharmacol., 221:107-111, "Interferon inducer, polyribogunanylic polyribocytidylic acid, inhibits experimental hepatic metastases in mice"	
	B14	Kawabe, Tsutomu et al., 1994, Immunity, 1:167-178, "The Immune Responses in CD40-Deficient Mice: Impaired Immunoglobullin Class . . . ".	
	B15	Kolanus, Waldemar et al., 1993, Cell, 74:171-183, "T Cell Activation by Clustered Tyrosine Kinases".	

Examiner Signature		Date Considered	

PTO/SB/08a/b (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet	3	of	4

Complete if Known	
Application Number	09/931,402
Filing Date	August 16, 2001
First Named Inventor	Jeffrey L. Browning
Art Unit	1642
Examiner Name	YAEN, CHRISTOPHER H
Attorney Docket Number	BINB185CPUSDV

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	C1	Kopp, William C. et al., 1993, J. of Immunother., 13:181-190, "Immunomodulatory Effects of Interferon--y in Patients with Metastatic Malignant Melanoma".	
	C2	Lane, Peter et al., 1992, Eur. J. Immunol., 22:2573-2578, "Activated human T cells express a ligand for the human B cell-associated antigen CD- 40 which participates in T cell-dependent activationof B lymphocytes".	
	C3	Langer, Robert, 1982, Chemtech. 12:98-105, "Controlled release of macromolecules".	
	C4	Langer, Robert, Brem, Henry et al., 1981, J. of Blomed. Materials, 15:267- 277, "Biocompatibility of polymeric delivery systems for macromolecules".	
	C5	Ling, Leona et al., 1995, J. of Interferon and Cytokine Res., 15:53-59, "Human Type I Interferon Receptor, IFNAR, Is A Heavily Glycosylated 120- 130 kD Membrane Protein".	
	C6	Loetshcer, Hansruedi et al., 1991, J. of Biolog. Chem., 266:18324-18329, "Recombinant 55-kDa Tumor Necrosis Factor (TNGF) Receptor".	
	C7	Morrison, Sherle et al., 1984, Pro. Natl. Acad. Sci., 81:6851-6855, "Chimeric human antibody molecules: Mouse antigen-binding domains . . . ".	
	C8	Niederle, Norbert et al., 1993, Leuk. Lymphoma, 9:111-119, "Long-Term Treatment of Chronic Myaelogenous Leukemia with Different Interferons: Results from Three Studies".	
	C9	Onishi, Tetsuro et al., 1994, Acta. Urol. Jpn., 40:195-200, "A Study On Direct Antitumor Activity of Bropirimine (Oral Interferon Inducer) For Renal Cell Carcinoma".	
	C10	Pleskov, V.M. et al., 1994, pp. 125-128, "Receptor-Mediated Endocytosis of Influenza Viruese and Low Density Lipoproteins by Tissue Cells".	
	C11	Queen, Cary et al., 1989, Proc. Natl. Acad. Sci., 86:10029-10033, "A Humanized antibody that binds to the interleukin 2 receptor".	
	C12	Raitano, Arthur B. et al., 1990, J. of Biol. Chem., 265:10466-10472, "Tumor Necrosis Factor Up-Regulates y-Interferon Binding in a Human Carcinoma Cell Line".	
	C13	Schiller, Joan et al., 1991, Cancer Research, 51:1651-1658, "Biological and Clinical Effects of Intravenous Tumor Necrosis Factor-alpha Administered Three Times Weekly".	
	C14	Schoenfeld, Hans-Joachim et al., 1991, J. of Biol. Chem., 266:3863-3869, "Efficient Purificationof Recombinant Human Tumor Necrosis Facotr Beta from Escherichia coli Yields Biologically Active Protein with a Trimeric Structure that binds to Both Tumor Necrosis Factor Receptors".	
	C15	Sidman, Kenneth et al., 1983, Biopolymers, 22:547-556, "Controlled Release of Macromolecules and Pharmaceuticals from Synthetic Polypeptides Based on Glutamic Acids".	

Examiner Signature		Date Considered	

PTO/SB/08a/b (08-03)
Approved for use through 07/31/2006. OMB 0651-0031
U.S. Patent and Trademark Office; U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449A/B/PTO

INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(Use as many sheets as necessary)

Sheet	4	of	4

Complete if Known	
Application Number	09/931,402
Filing Date	August 16, 2001
First Named Inventor	Jeffrey L. Browning
Art Unit	1642
Examiner Name	YAEN, CHRISTOPHER H
Attorney Docket Number	BINB185CPUSDV

NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No.[1]	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T[2]
	D1	Stepushkin, A.N. et al., 1994, pp. 131-134, "Comparative Studies of Live and Inactivated Influenza Vaccines: Organization of the Observations and the Results of Studies of Reactogenicty and Immunogenicity".	
	D2	Traunecker, Andre et al., 1989, Nature, 339:68-70, "Highly efficient neutralizationof HIV with recombinant CD4-immunoglobulin molecules".	
	D3	Ullrich, Axel et al., 1990, Cell, 61:203-212, "Signal Transduction by Receptors with Tyrosine Kinase Activity".	
	D4	Winter, Greg el al., 1991, Nature, 349:293-299, "Man-Made antibodies".	
	D5	Xu, Jianchao et al., 1994, Immunity, 1:423-431, "Mice Deficient for the CD40 Ligand".	
	D6	Yonehara, Shin et al., 1989, J. Exp. Med., 169:1747-1756, "A Cell-Killing Monoclonal Antibody (Anti-Fas) To A Cell Surface Antigen Co-Downregulated With The Receptor Of Tumor Necrosis Factor".	

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

[1]Applicant's unique citation designation number (optional). [2]Applicant is to place a check mark here if English language Translation is attached.

Examiner Signature		Date Considered	